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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/531,242

05/24/2005

Ashok Venkitaraman

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EXAMINER

KIM, ALEXANDER D

ART UNIT

PAPER NUMBER

1656

MAIL DATE

DELIVERY MODE

01/22/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/531,242

Applicant(s)

VENKITARAMAN ET AL.

Examiner

Alexander D. Kim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20 and 22-36 is/are pending in the application.
- 4a) Of the above claim(s) 26-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20 and 22-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☒ Other: Supplemental IDS (4/14/05).

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on 07/02/2007), Applicants filed a response and amendment received on 11/02/2007.. Said amendment cancelled Claims 1-19 and 21; amended Claims 20, 22 and 25.

Claims 20 and 22-36 are pending in the instant Office action. Claims 26-33 are withdrawn as non-elected inventions.

Thus, Claims 20 and 22-25 will be examined herein.

Response to the Request by Applicants.

2. Applicants requested a completely-initialed copy of the PTO-1449 because the reference WO 98/20030 reference does not have Examiner's initial, and the International Search Report of PCT/GB03/04485 has been crossed out with hand written comment of "wrong ISP".

The only ISP filed in the instant application is the ISP for PCT US97/20012 and the copy of ISP for PCT/GB03/04485 was not provided. That is why it was crossed out with comment of "wrong ISP". The missing initial for WO 98/20030 has been added and the supplemental IDS with the Examiner's initials has been attached in this office action.

Priority

3. Applicants requested clarification on why a certified copy of the foreign priority document is required when the instant application is 371 and the Notice of Acceptance

dated June 28, 2006 in the record indicated that said foreign priority has been filed in the PCT application.

The examiner acknowledge the certified copy of foreign priority of 0223860.8 (United Kingdom, filing date of 10/14/2002) has been filed in the PCT/GB03/04485.

Withdrawn- non Compliance with Sequence Rules

4. The previous non-compliance with sequence rules for the Figure 7 (d) is withdrawn by the applicants' argument.
5. The previous non-compliance with sequence rules for the polypeptide of FHTA on page 5, line11, is withdrawn by the applicants' argument.
6. The previous non-compliance with sequence rules for the polypeptide of "(ThrGlySer)4MetGly" on page 32, line2, is withdrawn by the applicants' argument.
7. The previous question regarding instant sequence listing disclosing many names other than the instant inventors on the first page is withdrawn by virtue of newly filed sequence listing on 11/02/2007.
8. The previous non-compliance with sequence rules statement that the content of the paper and CRF copies are the same is withdrawn by virtue of disclosing such statement in the Remarks filed on 11/02/2007.

Maintained-Compliance with Sequence Rules

9. The previous non-compliance with sequence rules is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue the structural coordinates in Figure 1 do not teach an amino acid sequence within the definitions of the Sequence Listing Rules. Thus, Figure 1 is a table of atomic coordinates - not a sequence to be listed in a sequence listing as defined by the Patent Office Sequence Listing Rules. However, the list of amino acids in Figure 1 teaches an amino acid sequence(s) longer than 4 amino acid; thus, it must comply with the sequence rules.

10. The previous non-compliance with sequence rules is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants recite "the specification has been revised to include the attached Sequence Listing which includes the Leu1521 to Glu1548. However, it is still unclear which SEQ ID NO have the amino acid sequence in the Table 3 having the sequence from Leu1521 to Glu1548. Further, it is unclear of the positions of 1521 and 1548 because the position is relative without the point of reference.

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11. Applicants failed to provide an amendment specifically directing the entry of newly filed copy of the sequence listing and/or CRF into the application, as shown in the previous Notice to Comply.

12. The appropriate change has to be made in the paper copy of sequence listing as well as CRF, because the SEQ ID NO: 20 has been determined to be a new matter. See new matter rejection below.

Withdrawn-Objections to the Specification

13. The previous objection of specification because the title is not descriptive of the claims is withdrawn by virtue of Applicants' amendment.

14. The previous objection of specification because the Abstract is withdrawn by virtue of Applicants' amendment.

15. The previous objection of specification regarding the inventorship between the PCT/GB2003/004485 and the instant application is withdrawn by virtue of Applicants' argument.

Withdrawn-Claim Rejections - 35 USC § 112

16. The previous rejection of Claim 22 under 35 U.S.C. § 112, second paragraph, the phrases "a resolution of better than 2.0" is withdrawn by virtue of Applicants' amendment.

New-Claim Objections

17. Claim 1 is objected to because of the following informalities: Claim 1 recites "a RAD51-BRC2 BRC4" whereas the instant specification recites "a RAD51-BRCA2 BRC4" on page 32, line 17. Appropriate clarification is required.

Maintained-Claim Rejections - 35 USC § 112

18. The previous rejection of Claims 20 and 22-25 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

The rejection was stated in the previous office action as it applied to previous Claims 20-25. In response to this rejection, applicants have amended Claims 20, 22 and 24-25; cancelled Claim 21 and traverse the rejection as it applies to the newly amended claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue the amended Claim 20 is believed to address points 1 to 3 on page 9 of the previous Office Action. Applicants also argue the teaching of Liu et al. and Yuan et al. appears to support the written description requirements.

The claim 20 satisfy two of three points on page 9 of the previous office action, that is the space group and the unit cell dimensions of the crystal. However, the Claim 20 failed to disclose the composition of the "RAD51-BRC2 BRC4" repeat sequence. As written, the genus of crystal comprising any sequence of RAD51, BRC2 and BRC4. In view of overly broad claimed crystal, the teachings of Liu et al. and Yuan et al. are considered as examples within the scope of claimed crystal but not enough to sufficiently represent the correlation between the structure of amino acids and the function of forming a crystal having orthorhombic space group $P2_12_12_1$ and unit cell dimensions $a=57.30 \pm 5\%$, $b=59.14 \pm 5\%$, $c=77.20 \pm 5\%$. One skilled in the art would not know which amino acid sequence is encompassed by the claimed polypeptide designated by the term "RAD51-BRC2 BRC4", "RAD51-BRC" or "RAD51 paralogue-BRC" and would not be able to possess the crystal thereof and further having said space group and unit cell dimensions. Claim 22 encompasses a crystal of Claim 20 with additional limitation of said resolution having a genus of polypeptide composition. Claim 23 also have not met all three requirement because "having --- Table 1" has been interpreted as "comprising --- Table 1" which encompasses any polypeptide comprising the coordinates of Table 1 with open structural limitation.

Applicants argue there is no suggestion that other RAD51-BRC repeat sequence or RAD51 paralogue-BRC repeat sequence chimaeras cannot be formed in a similar way and one of ordinary skill in the art would be able to make and use the claimed invention. This argument is related to a possession of a polypeptide which have

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different written description issues compared to the claimed invention that is the protein crystal.

One of skill in the art would be unable to predict the structure (the amino acid sequence, for example) of other members of the genera by virtue of the disclosed species of the instant disclosure or the prior art. For the reasons above and the previous office action, the instant rejection is maintained.

19. The previous rejection of Claims 20, and 22-26 under 35 U.S.C. 112, first paragraph, scope of enablement, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

The rejection was stated in the previous office action as it applied to previous Claims 20-25. In response to this rejection, applicants have amended Claims 20, 22 and 24-25; cancelled Claim 21 and traverse the rejection as it applies to the newly amended claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue the amended Claim 20 is believed to address points 1 to 3 on page 9 of the previous Office Action. Applicants also argue the teaching of Liu et al. and Yuan et al. appears to support the scope of enablement requirements.

Applicants argue there is no suggestion that other RAD51-BRC repeat sequence or RAD51 paralogue-BRC repeat sequence chimaeras cannot be formed in a similar way and one of ordinary skill in the art would be able to make and use the claimed invention. As previously noted above, this argument is related to make and use of a

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polypeptide for one skilled in the art which have different scope of enablement issues compared to the claimed invention that is the protein crystal. One skilled in the art may be able to make and use claimed protein (or polypeptide), but that does not automatically enable one skilled in the art to make and use the protein crystal thereof.

The claim 20 satisfy two of three points on page 9 of the previous office action, that is the space group and the unit cell dimensions of the crystal. However, the Claim 20 failed to disclose the composition of the "RAD51-BRC2 BRC4" repeat sequence. As written, the genus of crystal comprising any sequence of RAD51, BRC2 and BRC4. Claim 22 encompasses a crystal of Claim 20 with additional limitation of said resolution having a genus of polypeptide composition. Claim 23 also have not met all three requirement because "having --- Table 1" has been interpreted as "comprising --- Table 1" which encompasses any polypeptide comprising the coordinates of Table 1 with open structural limitation. As noted in the previous office action, the instant crystal having the coordinates of Figure 1 and examples of prior arts by Liu et al. and Yuan et al. is encompassed by the broad genus claimed protein crystal. However, the specification and the prior arts do not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Thus, applicant has not provided sufficient guidance to enable one skilled in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is

unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

New-Claim Rejections - 35 USC § 112

20. Claim 25 is rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- (a) Claim 25 recites the limitation "the RecA homology domain". It is unclear if the claims are limited to the one species disclosed in the specification (Figure 7, for example) or to one of any other RecA homology domain from any source, for example. Which RecA homology domain is encompassed in the Claim 25? Appropriate Clarification is required.

21. Claims 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, new matter, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a RAD51-BRC repeat sequence chimaera protein or a RAD51 paralogue-BRC repeat sequence chimaera protein, wherein the BRC repeat sequence contains the residue sequence (F or Y)x(TorS)A(S or H or G)(G

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or S or N)(K or R or T), where x can be any residue, which limitations are not supported by the original disclosure. Applicants stated that the sequence above has support because "the consensus sequence at the foot of Figure 3 which shows the sequence Fx(T or S)AS(G or S or N)K; and the table of Figure 3 itself which indicates that Y can be an alternative for F1524, H or G can be alternatives for S1528, and R or T can be alternatives for K1530. The examiner acknowledge the consensus sequence of Fx(T or S)AS(G or S or N)K in the foot of Figure 3 as shown below (indicated by circle) but the table itself does not support that "Y can be an alternative for F1524, H or G can be alternatives for S1528, and R or T can be alternatives for K1530". Thus, the residue sequence (F or Y)x(TorS)A(S or H or G)(G or S or N)(K or R or T), where x can be any residue, is determined to have no support in the original disclosure. The applicant is advised to point out the support in the original disclosure or amend the instant claims.

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FIGURE 3

Table 3 Structure-based analysis of BRCA2 BRC sequence conservation.

	β β β						β β β				α α α α α α α																	
	L	L	G	F	H	T	A	S	G	K	K	V	K	I	A	K	E	S	L	D	K	V	K	N	L	F	D	E
D	2			1			2	3		1						8	1		6	2	2		1	2	1	8	17	
E	1	1					1		1	1	9	2				21	22		3	4	1	1	4			7	28	
K	1		1	1			1		39	20	12	1				10	2		1	8	44	27	12	2	1	9	1	
R		4		1	8			1	1	5	2	4	2	1	2				4	1		11	1	1		6	1	
H				6				6	1							3	4		5		1							
N	3	1	1					1	7	7	1	4				2	1	6	5	1	2	1	11			5		
Q		1		1	8	1				3	5	7				5	1		8			8				1	4	
S	3	7	12	17	7	2	33	8		3	13	39	2	13	28	4	2	11		3						14		
T		2	2	2	45	1	1	1	5		8	5				5	2	3	3		3	2			1		3	1
G	5	15	21				2	4	37	1						2		1				3	1	6				
A	6		7				1	46			5					4	8	15		3		19	1	1			1	
P	5	4					1			1	1																1	
C	3			2	3			2			1	5						1			2						1	
I		4	5		3	1				2	16	12				2	8		3				6	2			1	
L	6	16				1	3			2	6	7	1			1	38	3				1			17	17		
V	2	1	4				1	1	1		23	2	33	1			4	1		14	7		7		2	1		
M															4								4	7	6			
F	14		3	50							1	1	1				1	4	2				1	8	35			
W																									6			
Y	3			2	7														1				1					

Consensus:

G F x T A S G K o i x i S o o S L x K A K x i F o D
 S S S A V R a L E
 N S

Claim Rejections - 35 USC § 101

22. The previous rejection of Claims 24-25 under 35 U.S.C. §101 because the claimed invention is directed to non-statutory subject matter, is withdrawn by virtue of Applicants' argument.

Withdrawn-Claim Rejections - 35 USC § 102

23. The previous rejection of Claims 20-25 under 35 U.S.C. 102(a) as being anticipated by Pellegrini et al. is withdrawn by virtue Applicants' argument.

24. The previous rejection of Claim 24 under 35 U.S.C. 102(b) as being anticipated by Liu et al. is withdrawn by virtue Applicants' amendment.

25. The previous rejection of Claim 25 under 35 U.S.C. 102(b) as being anticipated by Yuan et al. is withdrawn by virtue Applicants' amendment.

New-Claim Rejections - 35 USC § 102

26. Claims 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Pellegrini et al. (21 November 2002, Nature, vol. 420, pages 287-293, as cited in the IDS).

The claim 24 and 25 have been determined to contain a new matter as described in the 35 USC 112, new matter, rejection above. Thus, the priority date for Claim 24 and 25 is the instant filing date of 05/24/2005.

The reference of Pellegrini et al. is considered as "by other" because the inventive entity is different from the instant inventive entity.

As noted above in the instant office action, the term, "chimaera protein" in Claim 24 or "parologue" in Claim 25 have been interpreted as the terms that open up the limitation (which is similar to the term "comprising") of the instant claimed crystal or said

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proteins wherein the recited terms are not defined by the instant specification as long as the BRC repeat sequence contains the residue sequence (F or Y)x(T or S)A(S or H or G)(G or S or N)(K or R or T), where x can be any residue. Claim 25 has the further limitation of RAD51 paralogue has at least 15% sequence identity with RAD51 in the RecA homology domain.

Pellegrini et al. teach a crystal of RAD51-BRCA2 complex as shown in Figure 1, page 288. The crystal have a space group $P2_12_12_1$ and unit cell dimensions of $a=57.30$, $b=59.14$, $c=77.20$ with a resolution of 1.70 Angstroms (see PDB data of 1nOw). Pellegrini et al. "covalently linked BRC4 to RAD51" for the fusion protein (see top of right column, page 287). The Table 1 of Pellegrini et al. teach an identical table as the instant Figure 3 shown above, identifying the consensus sequence Fx(T or S)AS(G or S or N)K. The limitation of "15% sequence identity with RAD51 in the RecA homology domain" encompasses any sequence having 15% identity to any homology domain in any RecA polypeptide. Also, because the polypeptide of Pellegrini et al. is a publication of the instant application, the protein of Pellegrini et al. is identical to the claimed RAD51-BRC repeat sequence. Thus, the crystal or protein of Pellegrini et al. meet the limitations of Claims 24-25.

Conclusion

27. Claims 20 and 22-25 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 11AM-7:30PM.

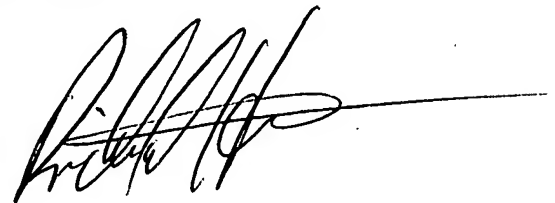
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim
9 January 2008

A handwritten signature in black ink, appearing to read 'Richard Hutson', with a long horizontal line extending to the right.

RICHARD HUTSON, PH.D.
PRIMARY EXAMINER